

INTERNATIONAL SEARCH REPORT

international application No
PCT/GB2006/002593

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/473 A61P25/14

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data bases consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2005/077946 A (CAMBRIDGE LAB LTD [GB]; TRIDGETT ROBERT [GB]; CLARKE IAN [GB]; TURTLE) 25 August 2005 (2005-08-25) page 5, line 20 - page 10, line 2 claims 1-34	1-16
X,P	WO 2006/053067 A2 (PRESTWICK PHARMACEUTICALS INC [US]; CLARENCE-SMITH KATHLEEN [US]) 18 May 2006 (2006-05-18) page 4, lines 5-20 page 5, lines 15-28	1-16

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *B* earlier document but published on or after the international filing date
- *C* documents which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *D* document referring to an oral disclosure, use, exhibition or other means
- *E* document published prior to the international filing date but later than the priority date claimed

- *F* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principles or theory underlying the invention
- *G* documents of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *H* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *I* document member of the same patent family

Date of the actual completion of the international search

20 November 2006

Date of mailing of the international search report

29/11/2006

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentsaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2140, Tx. 31 551 spo nl
Fax: (+31-70) 340-3018

Authorized officer

Young, Astrid

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C(Continuation), DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KILBOURN M R ET AL: "Absolute Configuration of (+)-alpha-Dihydrotetrabenazine, an Active Metabolite of Tetrabenazine" CHIRALITY, WILEY-LISS, NEW YORK, US, vol. 9, no. 1, 1997, pages 59-62, XP002329921 ISSN: 0899-0042 the whole document	1-16
A	KILBOURN M ET AL: "Binding of alpha-dihydrotetrabenazine to the vesicular monoamine transporter is stereospecific" EUROPEAN JOURNAL OF PHARMACOLOGY, AMSTERDAM, NL, vol. 278, no. 3, 1995, pages 249-252, XP002329922 ISSN: 0014-2999 the whole document	1-16

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 12-16 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/GB2005/002593

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WD 2005077946 A	25-08-2005	AU 2005213525 A1	25-08-2005
		CA 2555815 A1	25-08-2005
		EP 1716145 A1	02-11-2006
WD 2006053067 A2	18-05-2006	NONE	

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2006/002593

International filing date (day/month/year)
13.07.2006

Priority date (day/month/year)
14.07.2005

International Patent Classification (IPC) or both national classification and IPC
INV. A61K91/473 A61P25/14

Applicant
CAMBRIDGE LABORATORIES (IRELAND) LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399-0 Tx: 523658 epmu d
Fax: +49 89 2399-4465

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Young, Astrid

Telephone No. +49 89 2399-7811



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2006/002593

Box No. 1 Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 12-16

because:

☒ the said international application, or the said claims Nos. with respect to Industrial Applicability relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☐ no international search report has been established for the whole application or for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-16
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-16
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III:

1. Claims 12-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V:

2. The documents considered in the present processing are consecutively numbered D1-D4; this numbering results from the citations D1-D4 found in the International Search Report (ISR) of the corresponding PCT application. It will be adhered to in the rest of the procedure. The cited passage(s) for each citation will be considered unless otherwise specified.
3. The application refers to 3,11b-cis-dihydrotetrabenazine for use in halting or slowing the progress of one or more symptoms of Huntington's disease. Further, the use of 3,11b-cis-dihydrotetrabenazine in the preparation of a medicament for the treatment of one or more symptoms of Huntington's disease is claimed.
4. Novelty, Article 33(2) PCT
None of the cited prior art documents discloses compounds with the cis configuration at atoms 3 and 11 of dihydrotetrabenazine.

Thus, the subject-matter of claims 1-16 is considered novel within the meaning of Article 33(2) PCT.

5. Inventive Step, Article 33(3) PCT
The object underlying the present application is the provision of a medicament for halting or slowing the progress of one or more symptoms of Huntington's disease. The posed solution is the use of 3,11b-cis-dihydrotetrabenazine in the preparation of a medicament.

The use of tetrabenazine for the treatment of Huntington's disease has been known since long ago. It was further known, that the major metabolite is dihydrotetrabenazine, which is believed to be primarily responsible for the activity of

the drug. Hitherto only the trans isomers of 3,11b-dihydrotetraabenazine were known and used in medicine. However, the skilled person would have reasonably expected that also the cis-isomers show at least the same activity as the trans-isomers.

Thus, it is considered that the subject-matter of claims 1-16 does not involve an inventive step over the disclosure of D3 and D4 within the meaning of Article 33(3) PCT.

Re Item VI:

6. Certain published documents (Rule 70.10)
D1: WO 2005/077946 A (CAMBRIDGE LAB LTD [GB]; TRIDGETT ROBERT [GB]; CLARKE IAN [GB]; TURTLE) 25 August 2005 (2005-08-25)
D2: WO 2006/053067 A2 (PRESTWICK PHARMACEUTICALS INC [US]; CLARENCE-SMITH KATHLEEN [US]) 18 May 2006 (2006-05-18)

The above cited documents could become relevant for the assessment of novelty by entering the regional European phase.

Re Item VIII:

7. Claims 14 and 16 relate to a compound for use, method or use. These claims are considered unclear since they leave the reader in doubt about the category of the said claims, Article 6 PCT.